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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/776,865	02/02/2001	Carl G. Hellerqvist	22100-0100 (46126-252687)	7056

7590 09/06/2005

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EXAMINER	
RAWLINGS, STEPHEN L	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 09/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/776,865	HELLERQVIST, CARL G.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 June 2005 and 25 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-16,29-38,40-48,55 and 56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-16,29-38,40-48,55 and 56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 February 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 23, 2005 has been entered.

1. The amendment filed April 25, 2005 has been entered. Claims 49-54 have been canceled. Claims 1, 30, and 55 have been amended.

2. The declaration under 37 C.F.R. § 1.132 by Carl G. Hellerqvist, Ph.D., which was filed April 25, 2005, is acknowledged and has been entered.

3. Claims 1, 4-16, 29-38, 40-48, 55, and 56 are currently under prosecution.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restrictions

5. The inventions of Groups 1 and 11 have been rejoined. Furthermore, inasmuch as the requirement to elect a species of invention set forth in the Office action May 21, 2002 applies to the inventions of Groups 1 and 11, that requirement has been withdrawn.

Response to the Declaration

6. The merit of the declaration under 37 C.F.R. § 1.132 by Carl G. Hellerqvist, Ph.D., which was filed April 25, 2005, has been carefully considered but not found persuasive or sufficient to overcome the rejection of claims 1, 4-16, 29-38, 40-48, 55, and 56 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The reasons that the merit of

the declaration has not been found persuasive or sufficient to overcome this ground of rejection, based upon the inadequacy of the supporting disclosure of the claimed invention, are as follows:

Beginning at page 2 (item 3) of the declaration, Dr. Hellerqvist has declared that in the filed of cancer studies, mouse models are considered by those ordinarily skilled in the art as reasonably correlating with the human pathoangiogenic conditions, such as cancer. In response, Dr. Hellerqvist has provided no factual evidence to support this statement and it is aptly noted to contradict contrasting opinions by skilled artisans, which are based upon disclosed factual evidence. For example, Hoffman et al. (*Invest. New Drugs.* 1999; **17** (4): 343-359) discloses that currently used rodent tumor models do not sufficiently represent clinical cancer. Then, more recently, Peterson et al. (*European Journal of Cancer.* 2004; **40**: 837-844) states that although numerous candidate antitumor therapeutic agents have shown exciting activity in preclinical models, these agents often have had minimal activity clinically; see entire document (e.g., the abstract). As consequence of such poor extrapolation, Peterson et al. discloses there is reasonable skepticism about the true value of both syngeneic and xenograft rodent tumor models in accurately identifying agents that will be clinically useful (the abstract). Peterson et al. explains that there are many reasons why preclinical results do not predict human efficacy (page 837, column 2), but among those reasons are the pharmacokinetic differences between mouse and man (e.g., page 840, column 2, through page 841, column 2).

Furthermore, Dr. Hellerqvist has asserted that such mouse models are considered reasonably predictive of the therapeutic utility of compositons and methods for preventing or attenuating pathoangiogenic conditions, such as cancer. In apparent support of this assertion, Dr. Hellerqvist has referred to studies that were described at the 96th Annual Meeting of the American Association for Cancer Research held in 2005. In response, it is aptly noted that the only documentation provided in support of the assertion that mouse models are considered reasonably predictive of the therapeutic utility of compositions and methods for preventing or attenuating pathoangiogenic conditions, such as cancer, is a listing of the titles of presentations given during the 96th Annual Meeting of the American Association for Cancer Research held in 2005. The content of these presentations has not been disclosed to the Office; accordingly, the relevance of that content to the instant inquiry as to the sufficiency, or insufficiency, of the supporting disclosure to satisfy the enablement requirement set forth under 35 U.S.C. § 112, first

paragraph, cannot be assessed. Accordingly, while it is understood that Dr. Hellerqvist is skilled in the relevant arts, his assertion amounts to an unsubstantiated, albeit expert opinion, which contrasts markedly with the factual evidence of record cited in support of the Office's position. For example, contrary to the opinion stated in the declaration, Bodey et al. discloses that the failure of cancer vaccines to achieve clinically relevant therapeutic effects is, in part, due to the fact that preclinical studies using mouse models do not predict the efficacy of the vaccine when used to treat cancer in humans; see, e.g., pages 6 and 7 of the Office action mailed October 21, 2002.

At page 3 (item 4) of the declaration Dr. Hellerqvist states that disclosure would enable the skilled artisan to obtain compositions comprising one or more Group B hemolytic *Streptococci* (GBS) toxin receptors (i.e., HP59 or SP55), or immunogenic fragments thereof, and use such compositions to induce or maintain an immune response in a mammal to the GBS toxin receptors and thereby prevent or attenuate development of pathoangiogenic conditions, including cancer, in the mammal. In particular, Dr. Hellerqvist has referred to Example 6, provided in the specification at page 31, which exemplifies administering a composition comprising HP59 to mice, subsequently inoculating the mice with melanoma cells, and then comparing the survival of those mice to mice that were not immunized with HP59. However, the declaration provides no additional showings and accordingly the stated opinion is based entirely upon that which is disclosed in the instant application. As explained throughout prosecution, the amount of guidance, direction, and exemplification provided by the supporting disclosure is not reasonably commensurate in scope with the claimed subject matter and for reasons of record would not be sufficient to enable the skilled artisan to practice the claimed invention to attenuate any pathoangiogenic condition comprising cancer in any mammal without undue experimentation.

At page 3 (item 5) of the declaration Dr. Hellerqvist has referred to Fu et al. (of record), arguing that Fu et al. shows that the compositions to which the claims are directed are used to prevent or attenuate pathoangiogenic conditions, such as cancer. To the contrary, however, as noted in the previous Office action mailed July 26, 2004, Fu et al. actually provides factual evidence that compositions to which the claims are directed cannot be used to prevent cancer in mice; see the entire document, particularly Figure 6 at page 4192. Fu et al. vaccinated mice with HP59- and SP55-derived peptides and found that, while the growth of certain tumors (i.e., Lewis

lung tumors) was attenuated in the immunized mice, as compared that in to non-immunized mice, the immunization was not effective to prevent cancer (page 4192, Figure 6). While Fu et al. demonstrated that immunizing mice with peptides comprised of fragments of the amino acid sequence of HP59 or SP55 attenuated the growth of Lewis lung tumors in those mice, the claims are drawn to methods for attenuating a broad genus of "pathoangiogenic conditions comprising cancer". Thus, the showing of Fu et al. is not reasonably commensurate in scope with the claimed subject matter and for reasons of record, that showing would not reasonably convey to the skilled artisan that the supporting disclosure of the claimed invention is sufficient to enable one to use the claimed invention to attenuate any pathoangiogenic condition comprising cancer in any mammal without undue experimentation.

Furthermore, the declaration has noted that Fu et al. shows inhibition of Lewis lung tumor growth and reduced dissemination and growth of metastases and asserts that these are the criteria accepted by those of ordinary skill in the art in the field of cancer studies for characterization of effective prevention or attenuation of cancer. In response, Schuh (*Toxicol. Pathol.* 2004 Mar-Apr; 32 (Suppl.. 1): 53-66) teaches to the contrary that common reliance on survival and tumor burden data in a single mouse model often skews expectations towards high remission and cure rates, a finding that is seldom duplicated in clinical trials; see entire document (e.g., the abstract). Moreover, Schuh discloses "modulating and even curing experimental cancer in mice is a relatively easy process" (page 53, column 1); however, due to the inherent limitations of tumor models, these same treatment regimens lack efficacy in humans (e.g., abstract). Schuh explains, "[m]any commonly used mouse models of neoplasia have proven biased towards false positive results and preclinical studies have not accurately predicted clinical responses" (page 53, column 1). Schuh states, "[u]se of one or more simple models alone to determine possible clinical efficacy is contrary to the complexity and issues associated with tumor models in mice and the variation in accepted therapeutic protocols in clinical oncology" (page 61, column 1). Accordingly, as evidenced by Schuh and contrary to Dr. Hellerqvist's statements, the skilled artisan would not accept the showing of Fu et al. as demonstrating that the claimed compositions can be used to prevent or attenuate pathoangiogenic conditions, such as cancer.

Finally at page 4 (item 6) of the declaration Dr. Hellerqvist has referred to an abstract presented at the AACR Conference on Frontiers in Cancer Prevention Research in 2002 (i.e., Wamil et al.). The declaration states that Wamil et al. shows that a cancer vaccine comprising HP59-derived peptides is effective in preventing angiogenesis and pathology characteristic of cancer. Wamil et al. discloses that immunizing mice with peptides comprising fragments of the amino acid sequence of HP59 and SP55 and subsequently inoculating the mice with Lewis lung tumor cells attenuated the growth of tumors in those mice, as compared to controls. In addition, Wamil et al. discloses that mice immunized with these peptides became resistant to intravenous infusions of melanoma cells, as compared to controls. While Wamil et al. demonstrated that immunizing mice with such peptides attenuated the growth of Lewis lung tumors in those mice or conferred resistance to intravenous infusions of melanoma cells, the claims are drawn to methods for attenuating a broad genus of "pathoangiogenic conditions comprising cancer". Thus, the showing of Wamil et al. is not reasonably commensurate in scope with the claimed subject matter and for reasons of record, that showing would not reasonably convey to the skilled artisan that the supporting disclosure of the claimed invention is sufficient to enable one to use the claimed invention to attenuate any pathoangiogenic condition comprising cancer in any mammal without undue experimentation.

The declaration relies entirely upon limited amounts of data that were generated using two different mouse tumor models to support the assertion that the given the supporting disclosure, the skilled artisan could practice the claimed invention without undue experimentation. The problem with accepting such an assertion lies in the fact that the data generated using such mouse models cannot be reasonably extrapolated to reliably and accurately predict whether the claimed invention can be used to attenuate at least a substantial number of pathoangiogenic conditions comprising cancer and furthermore, as of yet, the clinical, therapeutic application of cancer vaccines to attenuate cancer has been met with very little success. In addition to references cited in preceding Office actions, which also describe such disappointing results and attribute the lack of success to various differences, such as the poor extrapolation of promising preclinical data to predict clinical efficacy, Wang et al. (*Exp. Opin. Biol. Ther.* 2001; 1 (2): 277-290) reviews the state of the art of T-cell-directed cancer vaccines for treatment of melanoma and states:

> Saved for scattered reports, however, the success of these approaches has been limited and T-cell-directed vaccination against cancer remains at a paradoxical standstill whereby anticancer immunisation can be induced but is not sufficient, in most cases, to induce tumour regression (abstract).

Wang et al. further states:

> Among the questions raised by this paradoxical observation [that systemic T-cell responses to vaccines often do not lead to objective clinical tumor regression] stands the enigma of whether tumour resistance to immunotherapy is due to insufficient immune response or because tumour cells rapidly adapt to immune pressure by switching into less immunogenic phenotypes [citations omitted].

In addition, Kelland (*Eur. J. Cancer.* 2004 Apr; **40** (6): 827-836) has reviewed the reliability of the model in predicting clinical response; see entire document (e.g., the abstract). While the successful use of such models in cytotoxic drug development is conclusive, Kelland discloses that today there is far less focus on the development of such drugs (page 833, column 2); rather, the focus is upon the development of "molecularly-targeted", largely cytostatic drugs, such as those disclosed in the instant application, which may act in synergy with other drugs to selectively reduce or inhibit the growth of neoplastic cells (e.g., page 885). In particular, where such drugs are naked humanized antibodies that act through mechanisms such as ADCC, Kelland states the models are of limited value, because such mechanisms depend upon the recruitment of the host's (i.e., mouse) immune response, which differs from or is not reflective of that found in man (page 834, column 2). With such limitations of the xenograft model in mind, Kelland suggests that the case for using the model within a target-driven drug development cascade need to be justified on a case-by-case basis (page 835, column 1). Still, Kelland et al. does not altogether discount the usefulness of such models, since, at present, "it is premature and too much a 'leap of faith' to jump directly from *in vitro* activity testing (or even in silico methods) to Phase I clinical trials (via preclinical regulatory toxicology)" (page 835, column 2). Kelland, however, does not advocate the use of a single xenograft model to exhort one to accept assertions of the effectiveness of treating multiple and different diseases using the same agent, as has been done in the instant application, since Kelland compels one to decide on a case-by-case basis whether such a model is suitable or not.

As noted in preceding Office action, Gura (of record) teaches that although researchers had hoped that xenografts would prove to better models for studying cancer in humans and screening candidate therapeutic agents for use in treating patient diagnosed with cancer, "the results of xenograft screening turned out to be not much better than those obtained with the original models". Gura states that as a result of their efforts, " '[w]e had basically discovered compounds that were good mouse drugs rather than good human drugs' ".

With further regard to the predictive value of various different preclinical models, Voskoglou-Nomikos et al. (*Clin. Cancer Res.* 2003 Sep 15; 9: 4227-4239) reports in a retrospective analysis that mouse allograft models were not predictive and xenograft models were only predictive for non-small cell lung and ovarian cancers, but not for breast or colon cancers; see entire document (e.g., the abstract).

Finally, Saijo et al. (*Cancer Sci.* 2004 Oct; **95** (10): 772-776) recently reviewed the reasons for negative phase III trial of molecular-target-based drugs and their combinations; see entire document (e.g., the abstract). Saijo et al. discloses that while numerous phase III trials have been conducted upon the basis of promising preclinical data such as that disclosed in the instant application, few have yielded strongly positive results, and the majority of results have been negative (e.g., abstract). Saijo et al. discloses that there are problems in preclinical prediction of combined effects of anticancer drugs, and the results of preclinical prediction of combined effects have been very poor (page 773, column 2). Saijo et al. teaches many reasons for the poor predictability of combined effects (page 774, Table 6).

Thus, taken collectively, there is a preponderance of factual evidence of record that the showing provided in the supporting disclosure would not enable the skilled artisan to practice the claimed invention without undue experimentation, as required under the provisions of 35 U.S.C. § 112, first paragraph.

Ground of Rejection Maintained

Claim Rejections - 35 USC § 112

7. The rejection of claims 1, 4-16, 29-38, 40-48, 55, and 56 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is maintained is maintained. The claim(s) contains subject matter which was not described in the specification in such a way

as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

At pages 8-11 of the response filed April 25, 2005, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

At page 9 of the amendment Applicant has asserted that the supporting disclosure of the claimed invention would be sufficient to enable the skilled artisan to make and use the claimed invention without undue experimentation because, in particular, the skilled artisan would consider the results of the examples provided, which used mouse models, predictive of the effectiveness of the claimed invention to attenuate any pathoangiogenic condition comprising cancer. In support of this assertion, Applicant has referred to Fu et al. (of record). Applicant's argument has been carefully considered but not found persuasive for the same reasons that the declaration was not found persuasive or sufficient to overcome this ground of rejection; those reasons are set forth above in section 9, headed "***Response to the Declaration***".

At page 10, Applicant has argued that claim 29 is allowable, since the claim does not recite any particular intended use, which is not sufficiently enabled by the supporting disclosure and when a compound is not limited by a recited use, any enabled use that would reasonably correlate with entire scope of the claim is sufficient to preclude a rejection for nonenablement based on how to use. In response, although Applicant has correctly noted that the subject matter of claim 29 is not include a recitation of intended use, it is noted that in the very next sentence Applicant has remarked, "Applicant respectfully asserts, and discusses in the previous section of this Response, that the disclosure of the present application enables one of ordinary skill in the art in the field of cancer studies, without undue experimentation, [...] to use the compositions to induce or maintain an immune response in a mammal to at least one of the Group B β-hemolytic Streptococci toxin receptors, and to prevent or attenuate development of pathoangiogenic conditions, including cancer, in a mammal" (paragraph bridging pages 10 and 11). Applicant has thus asserted that the present application enables a use of the composition recited in claim 29 and precludes a rejection for nonenablement based upon how to use. These remarks appear contradictory, since on the one hand it seems Applicant has argued there is some use for the

claimed composition other than in practicing the claimed methods, yet, on the other hand, Applicant has asserted that it is in practicing these methods that the skilled artisan would find the supporting disclosure adequately enabling.

If by these remarks Applicant has intended to suggest that the specification teaches the claimed compositions in fact have a use that is sufficiently enabled by the supporting disclosure, then, it is unclear what use that is. The claimed composition is disclosed as useful in preventing or attenuating a variety of pathologically and etiologically distinct and/or unrelated conditions or diseases, including, for example, psoriasis and arteriosclerosis; however, inasmuch as the claims are drawn to such methods and compositions useful in practicing such methods, the claims are directed to the subject matter of non-elected inventions. Inasmuch as the claims are directed to the subject matter of non-elected inventions, the merit of the supporting disclosure to enable the use of those inventions has not been considered, nor will be, during the prosecution of this application.

If by Applicant's remarks, Applicant has intended to suggest that there is some other use for the claimed compositions, apart from in practicing the elected invention, or even in practicing the non-elected inventions, it is aptly noted that the supporting disclosure provides no description of any other use. The term "composition", as it is used in the context of the claim language, is consistently and seemingly exclusively used in the disclosure in the context of describing a composition useful in preventing or attenuating a pathoangiogenic condition, such as cancer. In other words, apart from its disclosed usefulness in practicing the claimed method to prevent or attenuate diseases, disorders, or conditions, such as cancer, it appears the specification asserts no other use for the claimed composition.

Furthermore, it is duly noted that claim 30, which depends from claim 29, recites the composition of claim 29, wherein the receptors or fragments are in an amount effective for attenuating a pathoangiogenic condition in a mammal, wherein the pathoangiogenic condition comprises cancer"; therefore, the subject matter of claim 29 does in fact encompass compositions having the particularly recited intended use of claim 30. Nonetheless, as there is no other asserted use for the claimed composition, it is submitted that the only pertinent question asked in the instant inquiry is whether the claimed composition can be used in the manner that is asserted

by the specification, namely in preventing or attenuating a broad genus of pathoangiogenic conditions comprising cancer.

At page 11 of the amendment, Applicant has further commented that preceding Office actions have indicated that the supporting disclosure would be reasonably enabling for making and using, for example, a composition consisting of a mixture of Hab1, Hab2, and Hab3, or alternatively consisting of a mixture of p55a, p56a, p57a, Hab1, and Hab2 for attenuating tumor burden in mice subsequently challenged with melanoma or Lewis lung tumor cells, or reasonably enabling for claims drawn to a composition comprising "HP59/CFA" for protecting mice against the development of melanoma following the intravenous injection of melanoma cells; see, e.g., the scope of enablement rejection set forth in section 9 of the Office action mailed July 16, 2003. Applicant has contended that since the Office posed such compositions to be adequately enabled by the supporting disclosure, present claim 29 should be allowable over the requirements of the enablement provision set forth under 35 U.S.C. § 112, first paragraph. In response, claim 29 is not presently so limited. MPEP § 2164.01 states:

> The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Accordingly, even though the statute does not use the term "undue experimentation," it has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

Thus, there are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors, which have been outlined in the Federal Circuit decision of *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), include, but are not limited to, the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed. See also *Ex parte Forman*, 230 USPQ 546 (BPAI 1986). Although, given benefit of the supporting disclosure alone, claim 29 has embodiments

that might be used in particular applications without undue experimentation, because the breadth of the claims is a factor considered in this inquiry, claim 29 is not deemed to be sufficiently enabled by the supporting disclosure. The amount of guidance, direction, and exemplification set forth in the specification is not reasonably commensurate in scope with that of the claim and would not be adequate to enable the skilled artisan to use the better part of the breadth of the claimed subject matter in the asserted manner to attenuate a pathoangiogenic condition comprising cancer. Therefore, with regard to claim 29, this issue may be remedied by amending claim 29, such that it is limited to the embodiments that have been deemed adequately enabled by the supporting disclosure.

In conclusion, upon careful consideration of the factors used to determine whether undue experimentation is required, in accordance with the Federal Circuit decision of *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), there is a preponderance of factual evidence of record that indicates that the amount of guidance, direction, and exemplification disclosed in the specification, as filed, would not be sufficient to enable the skilled artisan to use the claimed invention at the time the application was filed without undue and/or unreasonable experimentation.

New Ground of Rejection

Claim Rejections - 35 USC § 112

8. Claims rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 4-16, 30-38, 40-48, 55 and 56 are indefinite because claims 1, 30, and 55 recite, "wherein the pathoangiogenic condition comprises cancer". Is the condition attenuated using the claimed invention cancer, or not? If not cancer, what is a pathoangiogenic condition comprising cancer? Perhaps cancer may be described as a pathoangiogenic condition; however, it is not conventional to describe a pathoangiogenic condition as comprising cancer. What condition or disease is attenuated in using the claimed invention? Is cancer attenuated, or is some other element of the pathoangiogenic condition attenuated? The answers to these questions cannot be gleaned from the disclosure, nor would the answers be apparent to the skilled artisan.

The metes and bounds of the subject matter that Applicant regards as the invention are not clearly and particularly delineated by the claim to permit the skilled artisan to determine what subject matter does or does not infringe the claim.

Claims 1, 4-16, 29-38, 40-48, 55, and 56 are indefinite because claims 1, 29, and 55 recite, "wherein the Group B β-hemolytic *Streptococci* toxin receptor comprises HP59 or SP55" and claim 55 recites, "wherein the Group B β-hemolytic *Streptococci* toxin receptor or immunogenic fragment thereof comprises HP59 or SP55". HP59 (i.e., the polypeptide of SEQ ID NO: 2) and SP55 (i.e., the polypeptide of SEQ ID NO: 4) *are* Group B β-hemolytic *Streptococci* toxin receptors; so, are the Group B β-hemolytic *Streptococci* toxin receptors to which the claims are directed HP59 or SP55, or not? The answer to this question cannot be gleaned from the disclosure, nor would the answer be apparent to the skilled artisan. With particular regard to claim 55, an immunogenic fragment of the Group B β-hemolytic *Streptococci* toxin receptor cannot comprise HP59 or SP55, because HP59 and SP55 are intact. Thus, the metes and bounds of the subject matter that Applicant regards as the invention are not clearly and particularly delineated by the claim to permit the skilled artisan to determine what subject matter does or does not infringe the claim.

9. Claims rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a "written description" rejection.

The considerations that are made in determining whether a claimed invention is supported by an adequate written description are outlined by the published Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, para. 1, "Written Description" Requirement (Federal Register; Vol. 66, No. 4, January 5, 2001). A copy of this publication can be viewed or acquired on the Internet at the following address: <http://www.gpoaccess.gov/>.

Claims 1, 4-16, 29-38, 40-48, 55, and 56 are directed to a genus of polypeptides that are Group B β-hemolytic *Streptococci* (GBS) toxin receptors or immunogenic fragments thereof

comprising HP59 and SP55. As explained above in the rejection of claims 1, 4-16, 29-38, 40-48, 55, and 56 under 35 U.S.C. § 112, second paragraph, because HP59 and SP55 are GBS toxin receptors, it cannot be understood how the GBS toxin receptors to which the claims are directed can be GBS toxin receptors or immunogenic fragments thereof that comprise HP59 and SP55. Accordingly, herein the claims are given the broadest reasonable interpretation, such that the GBS toxin receptors to which the claims are directed are not HP59 or SP55, but polypeptides that comprise amino acid sequences that are substantially identical (i.e., at least 80% identical, as defined by the specification) to those of either HP59 (SEQ ID NO: 2) or SP55 (SEQ ID NO: 4).

While the specification describes two polypeptides, namely the polypeptides of SEQ ID NO: 2 and SEQ ID NO: 4, the specification fails to describe how these polypeptides are representative of the genus, as a whole, to which the claims are directed. Moreover, the claims fail to recite and the specification fails to describe a particularly identifying (i.e., substantial) structural feature that is shared by the members of the genus of polypeptides to which the claims are directed, which correlates with a particularly identifying functional feature also common among members of the genus, such that it would be possible to immediately envision, recognize or distinguish at least a substantial number of those members. Therefore, the claims are directed to a genus of polypeptides that vary in substantially in both structure and function; yet, the specification only describes two such polypeptides. As such, the specification would not reasonably convey to the skilled artisan that Applicant had possession of the claimed invention at the time the application was filed.

Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, ``Written Description" Requirement (66 FR 1099-1111, January 5, 2001) states, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). "Guidelines" further states, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species *cannot* be achieved by disclosing only one species within the genus" (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure

of at least one species within the genus. Because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant had possession of the claimed invention at the time the application was filed.

The specification provides an adequate written description of nucleic acid molecules that comprise or consist of SEQ ID NO: 1, nucleic acid molecules that comprise or consist of the *full* complement of the nucleotide sequence of SEQ ID NO: 1 or the *full* complement of a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 2, nucleic acid molecules that *consist* of a polynucleotide sequence of SEQ ID NO: 1 (e.g., a nucleic acid molecule consisting of a fragment of SEQ ID NO: 1), and nucleic acid molecules that *consist* of a polynucleotide sequence that is complementary to the nucleotide sequence of SEQ ID NO: 1 (e.g., a nucleic acid molecule consisting of the full complement of a fragment of SEQ ID NO: 1).

However, the description of these few members of the claimed genus of nucleic acid molecules is not sufficient to meet the requirements of 35 USC § 112, first paragraph, since the genus embraces widely variant members and an adequate description of such cannot be achieved by describing members, which are not representative of the genus. As disclosed and claimed, the genus of nucleic acid molecules does not comprise members having a common, particularly identifying structural feature that correlates with a common functional feature shared by at least a substantial number of its members. As such, absent any of the factual evidence of an actual reduction to practice discussed above, the skilled artisan could not immediately envision, recognize, or distinguish at least a substantial number of the members of the claimed genus said at least substantial number. Accordingly, the specification would not reasonably convey to the skilled artisan that Applicant had possession of the claimed invention at the time the application was filed.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 29-34, 37, 38, 40-43, 45-48, 55, and 56 rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,803,448 B1.

The applied reference has a common assignee and a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

U.S. Patent No. 6,803,448 B1 ('448) teaches polypeptides that are identical to the polypeptides of SEQ ID NO: 2 and SEQ ID NO: 4; see entire document (e.g., SEQ ID NO: 4 and SEQ ID NO: 8 of the Sequence Listing). '448 teaches immunogenic fragments of such polypeptides, including, for example, the immunogenic fragment of the polypeptide of SEQ ID NO: 4 consisting of amino acids 9-35 of SEQ ID NO: 4; see, e.g., column 39, Table 8. '448 teaches making compositions comprising synthetic peptides and Freund's adjuvant, which are injected into rabbits to produce antibodies that bind to the polypeptides; see, e.g., columns 38 and 39, Example 3. Furthermore, '448 teaches the polypeptides are recombinant polypeptides produced in mammalian host cells; see, e.g., columns 24-26. '448 teaches the polypeptide are glycoproteins, or proteins that are naturally glycosylated; see, e.g., columns 19 and 20. Because the recombinant polypeptides are expressed in mammalian host cells (e.g., Chinese hamster ovary cells, HeLa cells), the recombinant polypeptides are glycosylated.

Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 29-32, 38, 40-43, 45-47, and 55 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 6,803,448 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons:

Claims 1-11 of the patent are directed to polypeptides comprising a mammalian GBS toxin receptor or immunogenic fragment thereof, particularly wherein the GBS toxin receptor is identical to the polypeptides of SEQ ID NO: 4 or SEQ ID NO: 8.

SEQ ID NO: 4 and SEQ ID NO: 8 of the patent's Sequence Listing are identical to SEQ ID NO: 4 (SP55) and SEQ ID NO: 2 (HP59), respectively, of the Sequence Listing of the instant application.

The claims of the instant application, on the other hand, are drawn to compositions comprising the polypeptides or immunogenic fragments thereof, to which the claims of the patent are drawn. Apart from this obvious difference, the claimed inventions are so substantially

similar that for the most part, the claimed subject matter of the patent anticipates the claimed subject matter of the instant application; and any other minor differences in the subject matter claimed in the instant application would be seen as an obvious variation of the subject matter claimed in the patent.

With regard to claim 31 of the instant application, it is noted that the claim recites the composition further comprises a "pharmaceutically acceptable carrier", which the instant specification defines as including, for example, water soluble formulations that comprise a buffer such as a phosphate buffer, or other organic acid salt, preferably at a pH of between about 7 and 8. It would be obvious to add a buffer to a water-soluble composition comprising the polypeptides to which the patent's claims are drawn.

With regard to claim 30, although the claim recites an intended use for the claimed composition, the composition itself cannot be materially or structurally distinguished from the obvious composition comprised of the polypeptides or immunogenic fragments thereof to which the patent's claims are directed. The recitation of intended use does not materially or structurally distinguish the claimed subject matter from the obvious variation of the subject matter to which the patent's claims are directed.

With regard to claim 38, which recites the polypeptides of which the claimed compositions are comprised are "recombinant or synthetic"; nevertheless, a composition comprising one or more of the polypeptides to which the patent's claims are directed cannot be materially or structurally distinguished from the claimed composition, because although the polypeptides of the claimed composition are "recombinant or synthetic", in this instance and absent a showing otherwise, the process by which the polypeptides are produced is not deemed to impart any material or structurally identifying or distinguishing feature.

Finally with regard to claim 55, the claim is drawn to a method for producing a composition comprising providing one or more of the proteins to which the patent's claims are directed and formulating a composition comprising the protein in a pharmaceutically acceptable excipient (e.g., a water soluble formulation comprising a buffer). The recitation of intended use of the material produced by the claimed process does not distinguish the claimed subject matter from the obvious process by which such a variation of the subject matter to which the patent's claims are directed is produced.

14. Claims 29-32, 38, 40-43, 45-47, and 55 are directed to an invention not patentably distinct from claims 1-11 of commonly assigned U.S. Patent No. 6,803,448 B1. Specifically, although the conflicting claims are not identical, they are not patentably distinct from each other for the reasons set forth above in the obviousness-type double patenting rejection of claims 29-32, 38, 40-43, 45-47, and 55.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned U.S. Patent No. 6,803,448 B1, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 35 U.S.C. 103(c) and 37 CFR 1.78(c) to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

Conclusion

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1643

slr
August 31, 2005